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Latent Trajectories of Common Mental Health Disorder Risk Across 3 Decades of Adulthood in a Population-Based Cohort

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IMPORTANCE Epidemiologic evidence indicates that most of the general population will experience a mental health disorder at some point in their lives. However, few prospective population-based studies have estimated trajectories of risk for mental disorders from young through middle adulthood to estimate the proportion of individuals who experience persistent mental disorder across this age period.

OBJECTIVES To describe the proportion of the population who experience persistent mental disorder across adulthood and to estimate latent trajectories of disorder risk across this age period.

DESIGN, SETTING, AND PARTICIPANTS A population-based, prospective cohort study was conducted between 1979 and 2008 in the canton of Zurich, Switzerland. A stratified random sample of 591 Swiss citizens was enrolled in 1978 at ages 19 years (men) and 20 years (women); 7 interviews were performed during a 29-year period. Men were sampled from military enrollment records and women from electoral records. From those initially enrolled, participants with high levels of psychiatric symptoms were oversampled for follow-up. Data analysis was performed from July 28, 2015, to June 8, 2016.

MAIN OUTCOMES AND MEASURES Latent trajectories, estimated using growth mixture modeling, of past-year mood/anxiety disorder (ie, major depressive episode, phobias, panic, generalized anxiety disorder, and obsessive-compulsive disorder), substance use disorder (ie, drug abuse or dependence and alcohol abuse or dependence), and any mental disorder (ie, any of the above) assessed during in-person semistructured interviews at each wave. Diagnoses were based on *DSM-III*, *DSM-III-R*, and *DSM-IV* criteria.

RESULTS Of the 591 participants at baseline, 299 (50.6%) were female. Persistent mental health disorder across multiple study waves was rare. Among 252 individuals (42.6%) who participated in all 7 study waves, only 1.2% met criteria for disorder every time. Growth mixture modeling identified 3 classes of risk for any disorder across adulthood: low (estimated prevalence, 40.0%; 95% CI, −8.7% to 88.9%), increasing-decreasing (estimated prevalence, 15.3%; 95% CI, 1.0% to 29.6%), and increasing (estimated prevalence, 44.7%; 95% CI, −0.9% to 90.1%). Although no classes were characterized by persistently high disorder risk, for those in the increasing-decreasing class, risk was high from the late 20s to early 40s. Sex-specific models indicated 4 trajectory classes for women but only 3 for men.

CONCLUSIONS AND RELEVANCE Persistently high mental health disorder risk across 3 decades of adulthood was rare in this population-based sample. Identifying early determinants of sex-specific risk trajectories would benefit prevention efforts.

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There exists a sizable body of evidence regarding lifetime prevalence of mental health disorder in the population. Estimates from large-scale, cross-sectional population surveys that were initially criticized for being too high[1-6] have been replicated[7,8] and followed by even higher estimates of cumulative risk from prospective studies[9-13] that repeatedly assessed mental health disorder over time. For example, prospectively generated prevalence estimates in the Baltimore site of the Epidemiologic Catchment Area (ECA) study were 2 to 12 times higher than those estimated retrospectively, corroborating the idea that retrospective assessment may underestimate mental health disorder frequency owing to reliance on recall.[12,14,15] Together, these studies imply that mental health disorder is commonly experienced in the population, although common experiences are not necessarily synonymous with severe disorder or treatment need.[3,4]

Despite ample evidence regarding lifetime prevalence, little is known about the persistence of aggregate mental health disorder across the lifespan. Although a number of studies, such as that of Colman et al,[16] have estimated trajectories of symptoms over time, descriptions of trajectories of mental health disorder are scarce. The few diagnostic studies[9,17-20] that have followed population-based samples of adults for more than 20 years have provided important information about the incidence and course of specific disorders. Along with longitudinal studies[19,21-29] of children followed into early adulthood, these indicate a substantial degree of heterogeneity in course and comorbidity with other mental health disorders over time. The combination of recurrence and comorbidity could imply that a sizable proportion of the population is at high risk for mental health disorder throughout most of the adult lifespan. Estimating this proportion in the general population would provide an indicator of public health burden and identify a subgroup in which targeted prevention strategies may have greater impact. Furthermore, identification of risk trajectories across adulthood would have implications for etiologic research, prevention, and treatment.

Although a few studies[30,31] have estimated trajectories of mental health disorder from childhood or adolescence through early adulthood, to our knowledge, no studies have estimated risk trajectories past age 30 years to assess the degree of persistence across the early to later stages of adulthood. Olino et al[31] found that only approximately 3.4% of participants in their study belonged to classes representing either persistent depression or persistent anxiety from ages 14 to 30 years. In the present study, we report on persistence and trajectories of risk of common mental health disorder across 29 years in the Zurich Cohort Study, a population-based cohort of young adults who were aged 20 (men) and 21 (women) (20/21) years in 1979 and interviewed about past-year mental health disorder 7 times between 1979 and 2008. The study aims were to (1) describe the frequency of repeated mental health disorder across time and (2) estimate latent classes of mental health disorder risk trajectories. To our knowledge, this is the only study to describe mental health disorder risk trajectories among a prospective cohort of same-aged individuals interviewed repeatedly across middle adulthood.

Key Points

Question What proportion of the general population experiences persistent mental health disorder across young to middle adulthood?

Findings In this population-based cohort study conducted in Switzerland, persistent mental health disorder across 7 waves of assessment from ages 20 (men) and 21 (women) (20/21) years to 49/50 years was uncommon. The most persistent trajectories identified reflected high risk from ages 27/28 years to 40/41 years, and trajectories differed between men and women.

Meaning Despite prior evidence for high lifetime prevalence of mental health disorder in the population, having persistent disorder across young to middle adulthood is rare.

Methods

Sample

The Zurich Cohort Study[32] is a population-based sample of young adult residents of the canton of Zurich, Switzerland. In 1978, a total of 2201 young men (aged 19 years) were randomly sampled at compulsory military enrollment (50% of the total 19-year-old male population; refusal rate, 0.3%). A total of 2346 young women (aged 20 years) were sampled from electoral registers the same year and contacted by mail (50% of the total 20-year-old female population; 75% response rate). These 4547 participants were screened (Symptom Checklist-90)[33] and divided into high (≥85th percentile) and low (<85th percentile) scorers based on the Global Severity Index.[34] To increase the likelihood of mental health disorders developing in the cohort, a stratified sample consisting of two-thirds high scorers and one-third low scorers was selected for follow-up. These 591 participants (299 [50.6%] women) were interviewed at 7 waves: 1979 (591 participants; aged 20/21 years), 1981 (456 participants; aged 22/23 years), 1986 (457 participants; aged 27/28 years), 1988 (424 participants; aged 29/30 years), 1993 (407 participants; aged 34/35 years), 1999 (367 participants; aged 40/41 years), and 2008 (335 participants; aged 49/50 years). Two hundred fifty-two participants (42.6%) completed all 7 interviews. The initial distribution of high and low scorers did not change during follow-up, but dropouts were more common among extreme high and low scorers and women participated more often than men.[35] eTable 1 in the Supplement provides information about the presence of prior mental health disorder in participants and nonparticipants at each follow-up wave. All participants provided written informed consent, and the study was approved by the institutional review board of the University of Zurich. There was no financial compensation.

Measures

Interviews were conducted with the Structured Psychopathological Interview and Rating of the Social Consequences of Psychological Disturbances for Epidemiology, a semistructured interview that used a bottom-up approach to

assess sociodemographics, 11 somatic and 13 psychiatric syndromes, substance use, medication use, health service use, impairment, social activity, and other factors.[32] Reliability and validity of the instrument have been reported.[36] Interviews were conducted by trained psychologists or psychiatrists with good interrater agreement (κ = 0.9 for major depression and generalized anxiety disorder[36]). Diagnoses were based on *DSM-III* (1979-1986), *DSM-III-R* (1988-1993), and *DSM-IV* (1999-2008),[37-39] without exclusion criteria. Herein, we present 2 disorder types: mood/anxiety and substance use. Mood/anxiety disorders include major depressive episodes and the following anxiety disorders: agoraphobia, social phobia, specific phobia, panic, generalized anxiety disorder, and obsessive-compulsive disorder. Substance use disorders include alcohol and drug abuse or dependence. Summary variables were created to indicate the past-year presence of any mental health disorder, mood/anxiety disorder, and substance use disorder at each wave, on which trajectories were based.

Statistical Analysis

All analyses were weighted to account for sample stratification. First, proportions were calculated to describe disorder persistence during the study period. Second, a single population average disorder trajectory was estimated using generalized estimating equations.[40] Models included categorical time, sex, and a time × sex interaction as predictors with unstructured correlation matrices. Main and interactive effects of sex were assessed using χ^2 tests ($\alpha = .05$).

Third, latent classes of trajectories of mental health disorder presence across adulthood were estimated. Latent variable methods that have been used to study the structure of mental health disorder comorbidity have traditionally been divided into person-centered (eg, latent class analysis) and variable-centered (eg, factor analysis) approaches.[41] The latter approaches have often found that mental health disorders are described by 2 factors—an internalizing (mood and anxiety) and an externalizing (behavior and substance use) factor—with comorbidity occurring both within and between domains.[42-44] Person-centered approaches aim to identify homogeneous latent subgroups within a heterogeneous population. We used one such technique, growth mixture modeling (GMM), because we were interested in identifying groups rather than investigating the structure of comorbidity. We performed GMM using MPlus, version 6.1,[45] to empirically classify participants into subgroups or classes that share a common trajectory of mental health disorder risk over time. All available data were included in the analysis, and missing data were handled by full information maximum likelihood, which assumes that missingness is random given the observed data.[46] We first estimated latent trajectories of any disorder in the full sample by comparing the following 1-class through 4-class models: linear change over time without within-class intercept variance (linear latent class growth analysis), quadratic latent class growth analysis, and quadratic change over time with within-class intercept variance (quadratic GMM). Intercept variance was constrained to be equal across classes. Fit statistics are presented in eTable 2 in the Supplement. Because of data sparseness, some complex models were not well identified and therefore were not considered further. Model selection focused on information criteria (IC), including Akaike IC,[47] Bayesian IC,[48] and sample size–adjusted Bayesian IC (ABIC),[49] as well as model interpretability. ABIC was given priority because of previous studies[50,51] indicating that it outperforms other IC, especially when small classes are present. The lowest IC were observed for the 3-class quadratic GMM, which was selected to represent trajectories of any disorder across adulthood. Fit was not improved by allowing random slopes within classes or variation in intercept variance across classes.

We next estimated trajectories by sex and disorder type. We repeated the 1- through 4-class quadratic GMMs for mood/anxiety disorders and substance use disorders as well as for any disorder among men and women separately. Because of greater variability in the data for women than for men, reduced model complexity among men was allowed by removing quadratic growth factors and/or within-class intercept variance. Greater variability among women was accommodated by allowing models to have more classes as long as identification problems were not encountered.

The relatively small sample and low classification precision precluded systematic assessment of specific correlates of trajectory class. However, for interested readers we provide some class characteristics based on most likely class membership (eTable 3 in the Supplement). These analyses are considered exploratory and are not appropriate bases for inference.

Results

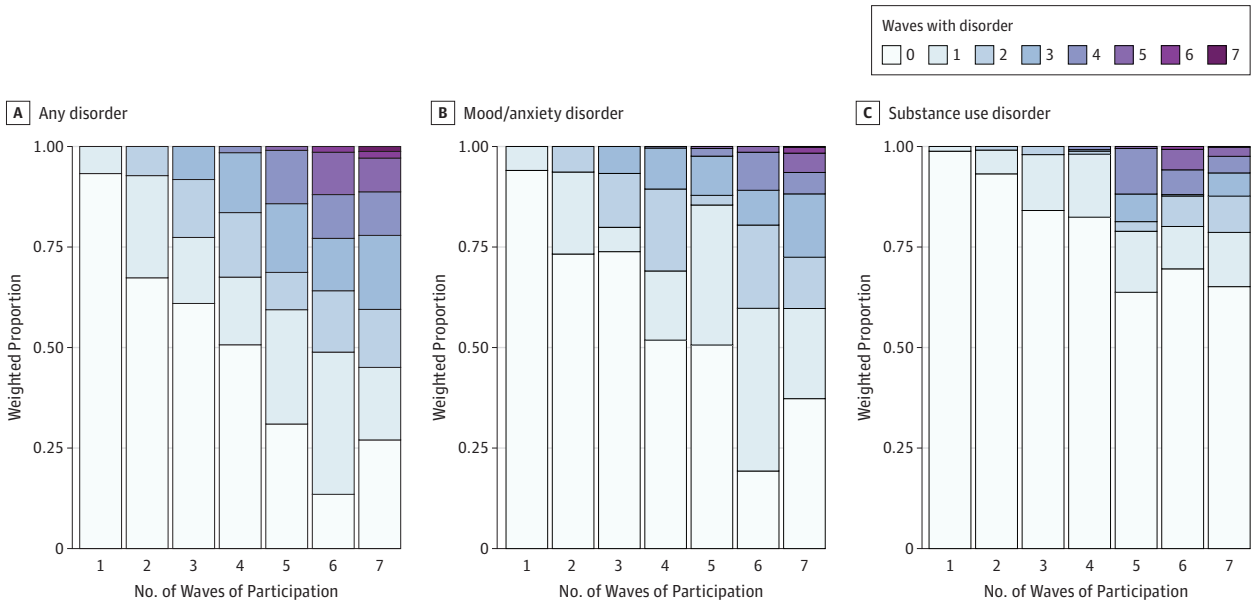
Disorder Persistence

Figure 1 displays the weighted proportions of participants with a past-year mental health disorder at 0 through 7 waves by the number of waves of study participation, which could have been nonconsecutive. This information is displayed in tabular format in eTable 4 in the Supplement. Among individuals who participated in 6 and 7 waves, 1.4% and 2.9%, respectively, met diagnostic criteria at least 6 times, and 12.0% and 11.3%, respectively, received a past-year diagnosis at 5 or more waves. Among those who participated in all study waves, only 1.2% met criteria for a disorder at every interview; 0.2% met criteria for a mood/anxiety disorder every time, and no participants met criteria for a substance use disorder every time. The distribution of the percentage of participated waves in which a disorder was present is displayed in the eFigure in the Supplement. Approximately 31% of the participants met criteria for any disorder at 2 consecutive waves and approximately 15% met criteria at 3 consecutive waves (eTable 5 in the Supplement).

Population Average Trajectory

Predicted weighted past-year prevalence of any disorder, mood/anxiety disorder, and substance use disorder for men and women are displayed in **Figure 2**. For all 3 disorder types, past-year prevalence tended to be lower in the early 20s and fluctuate at moderate levels afterward. The exception to this finding was substance use disorder among women, which was most prevalent at ages 28 and 50 years and rare at 30 years.

Figure 1. Persistence of Past-Year Mental Health Disorder by Number of Waves of Study Participation



Any disorder (A), mood/anxiety disorder (B), and substance use disorder (C) at 0 through 7 study waves by number of waves of participation. Fifty-one individuals participated in 1 wave, 50 in 2 waves, 44 in 3 waves, 55 in 4 waves, 64 in 5 waves, 75 in 6 waves, and 252 in all 7 waves.

For any disorder and mood/anxiety disorder, there were main effects of sex, with women having higher odds of a disorder at age 20/21 years, but trajectories of disorder across time did not differ significantly by sex (any disorder, $\chi^2_6 = 7.41$, $P = .28$; mood/anxiety disorder, $\chi^2_6 = 8.80$, $P = .19$). The opposite was true for substance use disorder: the odds of disorder at age 20/21 years did not differ significantly by sex ($\chi^2_1 = 2.84$, $P = .09$ odds ratio [OR], 0.23; 95% CI, 0.04-1.27), but the trajectory of disorder across time differed significantly ($\chi^2_6 = 17.04$; $P = .009$).

Latent Trajectories

The best-fitting model for any disorder in the full sample was a 3-class quadratic GMM (**Figure 3**A). All 3 classes had low (0.09-0.21) estimated probabilities of any disorder at ages 20/21 to 22/23 years. The low class (estimated prevalence, 40.0%; 95% CI, −8.7% to 88.9%) had relatively low probability of mental health disorder throughout adulthood, which was highest (0.23-0.24) at ages 27/28 to 29/30 years. The increasing-decreasing class (estimated prevalence, 15.3%; 95% CI, 1.0% to 29.6%) had high probabilities (0.76-0.93) from the late 20s to early 40s that decreased to 0.42 by 49/50 years. The increasing class (estimated prevalence, 44.7%; 95% CI, −0.9% to 90.1%) displayed increasing probabilities across adulthood that ended at 0.72 at 49/50 years.

The best-fitting model (by ABIC and AIC) for mood/anxiety disorders in the full sample was also a 3-class GMM (Figure 3B). The trajectories are similar to those for any disorder. Again, all 3 classes had low estimated probabilities (0.09-0.12) of mood/anxiety disorder at ages 20/21 to 22/23 years. Estimated prevalence was 48.4% for the low class (95% CI, 20.2% to 76.5%), 8.7% for the increasing-decreasing class (95% CI, −3.0% to 20.4%), and 42.9% for the increasing class (95% CI, 10.4% to 75.4%). Estimated probabilities for the increasing-decreasing class were highest (0.89) at age 34/35 years.

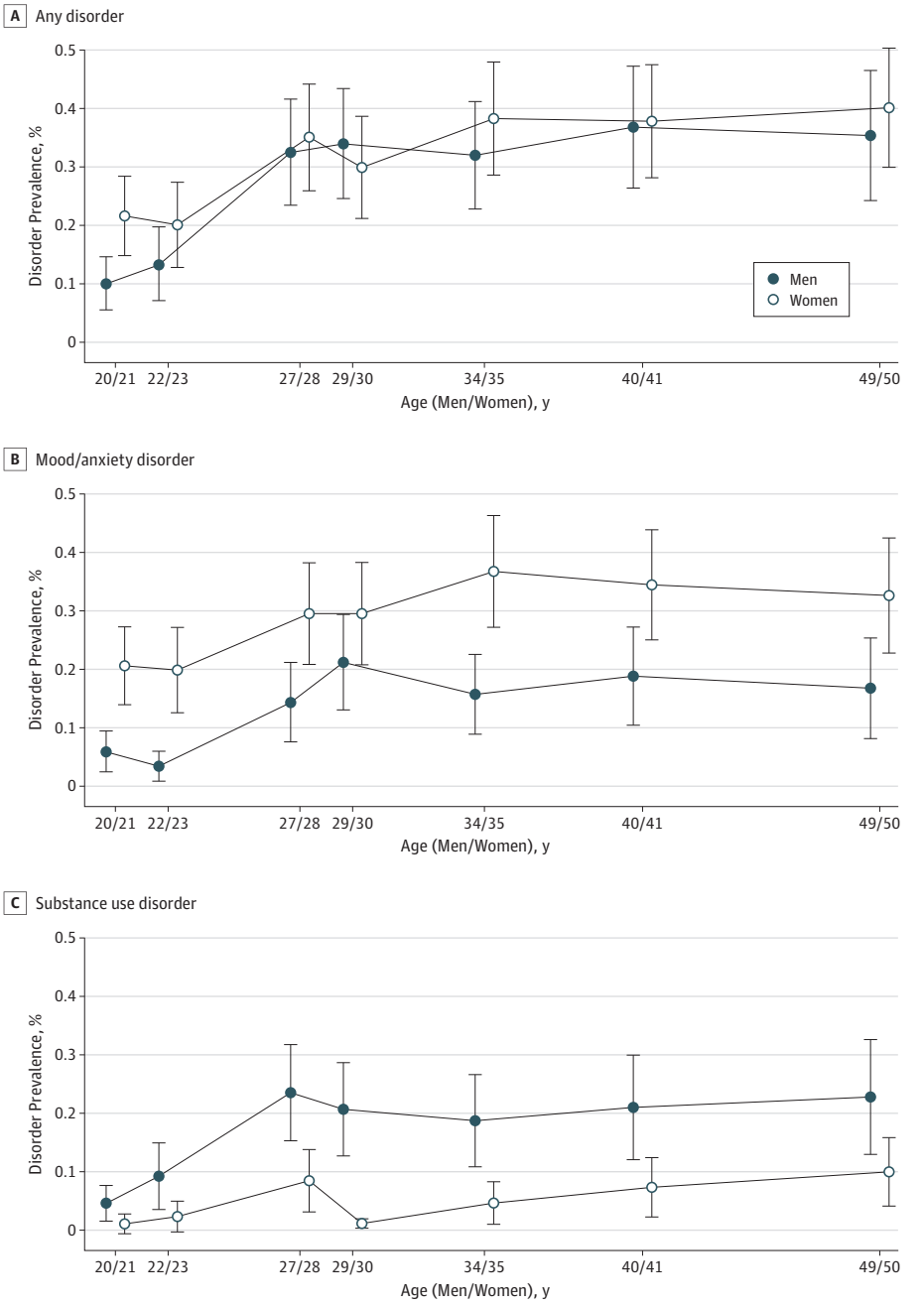
The best-fitting model for substance use disorders in the full sample was the 2-class GMM (Figure 3C). This model contained only a low class (estimated prevalence, 74.5%; 95% CI, 62.0%-87.0%) and an increasing-decreasing class (estimated prevalence, 25.5%; 95% CI, 13.0%-38.0%). The highest estimated probability for the increasing-decreasing class was 0.50 at age 34/35 years.

Trajectories by Sex

The best-fitting model for any disorder among men was a 3-class latent class growth model with a quadratic term specified for only 1 class (**Figure 4**A). The largest of these was the low increasing class (estimated prevalence, 71.1%; 95% CI, 57.1%-85.1%), which had probabilities of any disorder close to 0.10 through age 29 years that increased gradually to 0.31 by age 49 years. The increasing-decreasing class had an estimated prevalence of 21.3% (95% CI, 6.2%-36.4%) and a peak estimated probability of 0.77 at age 34 years. The early increasing class (estimated prevalence, 7.6%; 95% CI, 0.2%-15.0%) had a low estimated probability (0.09) at age 20 years that increased steeply thereafter.

The best-fitting model for any disorder among women was a 4-class GMM (Figure 4B). In this model the low class (estimated prevalence, 28.8%; 95% CI, 13.5%-44.0%) had probabilities of any disorder close to zero throughout adulthood. The increasing-decreasing class had an estimated prevalence

Figure 2. Predicted Prevalence of Past-Year Mental Health Disorder Across Age



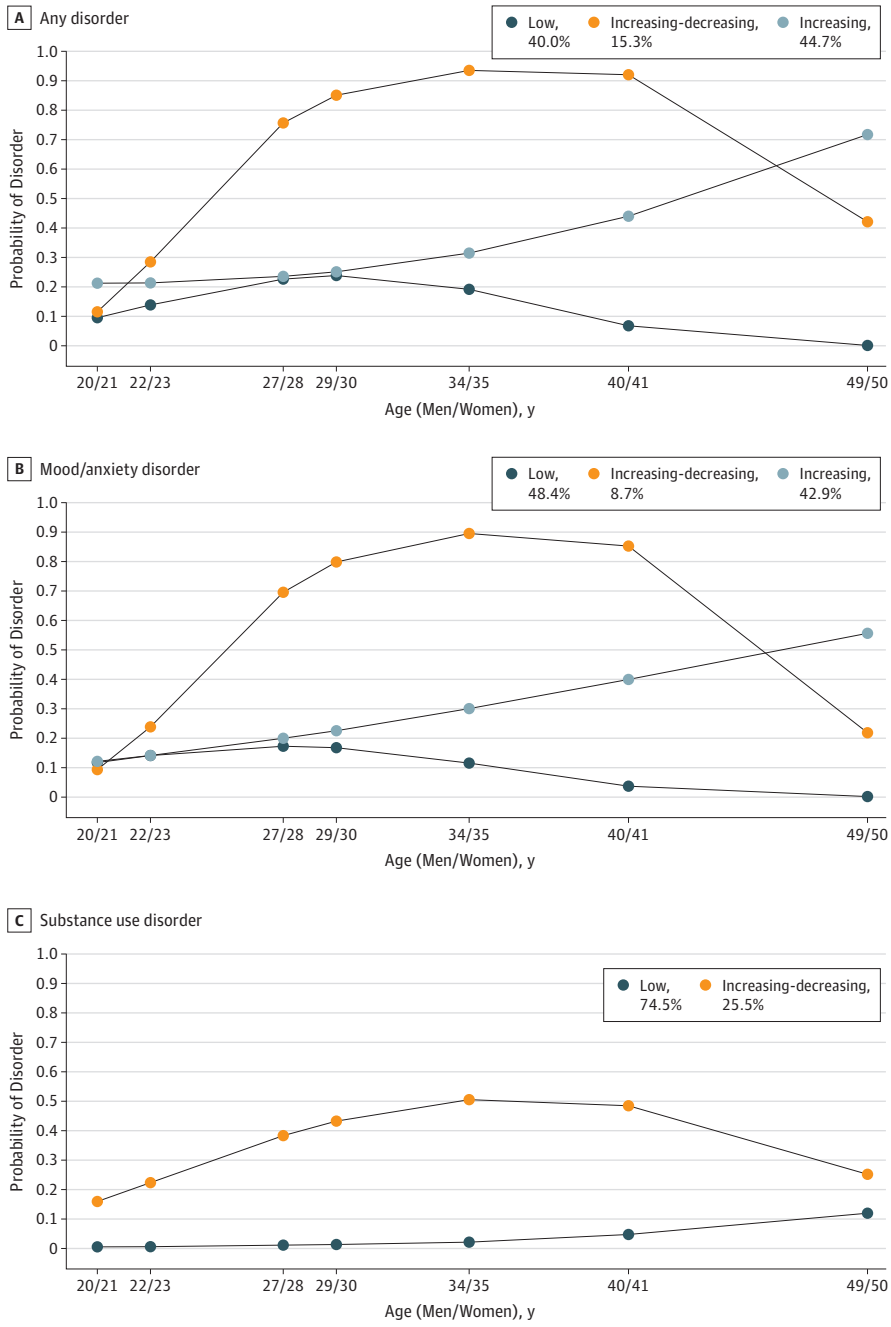
Weighted predicted prevalence of any disorder (A), mood/anxiety disorder (B), and substance use disorder (C) shown by age and sex. Error bars indicate 95% CIs.

of 15.6% (95% CI, 5.5%-25.6%) and a peak estimated probability of 0.91 at 35 years. The increasing class, comprising an estimated 37.8% (95% CI, 19.9%-55.7%) of women, had probabilities close to 0.33 from 21 to 30 years that increased thereafter to 0.95 at 50 years. The decreasing class (estimated prevalence, 17.8%; 95% CI, 2.9%-32.8%) also had moderate probabilities (0.29-0.42) from ages 21 to 30 years that decreased thereafter and were close to zero at 50 years. Estimated probabilities of mental health disorder at each wave in each model are displayed in eTable 6 in the Supplement.

Discussion

This study estimated persistence and latent classes of trajectories of risk for common mental health disorders across early to middle adulthood among a population-based cohort interviewed 7 times between ages 20/21 and 49/50 years. Among those who participated in 4 or more study waves, the proportion who met diagnostic criteria at every interview ranged from 0.9% to 1.5%. The infrequency of persistent disorder was also

Figure 3. Latent Trajectories of Past-Year Mental Health Disorder Risk by Disorder Type

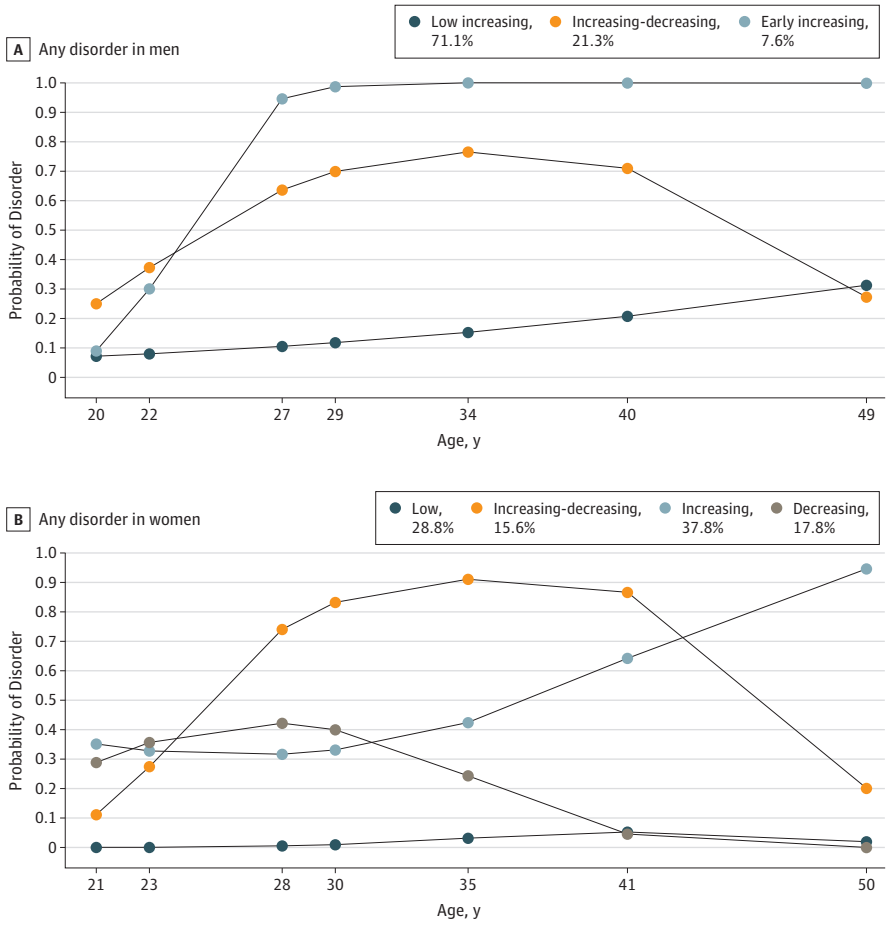


Growth mixture models of any disorder, using a 3-class model (A); mood/anxiety disorder, using a 3-class model (B); and substance use disorder, using a 2-class model (C) across age.

evident in the latent trajectory models; no classes characterized by consistently high probability of disorder across time were identified. Similar to a study[31] of trajectories from adolescence to 30 years, our results indicate that, despite high lifetime prevalence estimates from community surveys, persistence across young to middle adulthood is rare.

In the overall sample, we identified 3 latent classes: 1 whose risk of disorder remained low throughout the study, 1 whose risk increased with age, and 1 whose risk was high from the late 20s to the early 40s. This third class represented the most persistent trajectory identified, and this trajectory shape was identified in each model. Peak probabilities for this class appeared to be higher for mood/anxiety disorders than for substance use disorders and for women compared with men. This class may represent the most common form of persistence that occurs in the general population; class prevalence estimates ranged from 8.7% for depression/anxiety to 25.5% for substance use disorder. Peak probabilities in the increasing-decreasing trajectories coincide with the median age at onset for depression reported in the Lundby Study[23] and the Baltimore ECA study,[21] as well as with ages of peak symptom levels for 3 of 6 classes described in a prior study[16] covering a

Figure 4. Latent Trajectories of Past-Year Mental Health Disorder Risk by Sex



Growth mixture models of any disorder in men, using a 3-class model (A), and women, using a 4-class model (B), across age.

similar age period. Peak ages also correspond to periods of workforce participation and child rearing, highlighting the potential for prevention efforts to mitigate the economic costs of mental health disorders as well as any environmental effects of parental depression on children.[52,53]

For any disorder overall, mood/anxiety, and any disorder among women, we found classes with increasing disorder risk over time. If this trajectory continues to increase into the 60s, this class may represent persons prone to late-life depression and anxiety. Intervening early in this trajectory might therefore reduce the burden associated with late-life disorder and its sequelae.[54]

There were differences in the latent trajectory models for any disorder estimated among men and women. More classes were estimated among women than among men, reflecting greater variability in response patterns that could be partly due to greater participation among women. Although increasing-decreasing classes were present among both sexes, the other trajectories differed in shape, complexity, and prevalence. The finding of different class structures by sex is consistent with known sex differences in risk for and course of mental health disorders[17,20,55,56] as well as neural development and processes.[57]

Differences in risk trajectory across the life course may reflect differences in etiology. Epidemiologic research focusing on a particular snapshot in time may therefore ignore etiologic heterogeneity due to the composition of risk trajectory types in the study population. In addition, different trajectories may be amenable to different clinical treatment approaches and prevention strategies. The realization of these implications will ultimately rely on trajectory prediction at the individual level. While we were unable to systematically assess predictors of trajectory class membership in this relatively small sample, our exploratory descriptive analyses, along with prior studies (eg, Musliner et al[58]) of specific disorders, imply that larger studies may be able to distinguish trajectories based on characteristics such as family history, distress, and comorbidity (eTable 3 in the Supplement). Such studies may enhance the utility of psychiatric diagnosis by leading to improved prediction of long-term outcomes[16,59] while simultaneously informing service planning and targeted prevention efforts.

Strengths of this study include the community-based sample, the prospective design that covered 3 decades of young to middle adulthood, and the phenomenologic approach to diagnosis. In addition, men and women were each sampled at a

single age at the start of the study, allowing us to estimate trajectories free from age effects. Finally, participants were repeatedly assessed for past-year mental health disorder, reducing errors arising from long recall periods.

Limitations of the study include the relatively small sample size and attrition over the long study period, which could have affected our estimates. These factors also reduced the complexity of the models that could be estimated. Therefore, more complex models, perhaps with a greater number of latent trajectories, may be identifiable in larger studies. However, we would conjecture that, if such models were to contain classes representing persistent mental health disorder, the prevalence of these classes would be low. Disorder episodes that started and ended between study waves were missed, which may have resulted in an underestimate of persistence. Uncommon disorders, such as schizophrenia, were not included. The study covers 3 decades of adulthood but not childhood, early adolescence, or later adulthood. Continued follow-up of population birth cohorts could generate valuable information about the continuity of trajectories of disorder risk across life stages. Finally, this study was conducted within a particular geographic location, possibly limiting generalizability.

Conclusions

Despite the apparently large proportion of the population that will experience mental health disorders at some point across their lives, our results indicate that a relatively small proportion will experience persistent disorder across multiple decades of adulthood. Research assessing correlates of risk trajectory across the lifespan may have substantial clinical and public health impact.

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Acquisition, analysis, or interpretation of data: Paksarian, Cui, Ajdacic-Gross, Rössler, Merikangas.
Drafting of the manuscript: Paksarian, Cui.
Critical revision of the manuscript for important intellectual content: Angst, Ajdacic-Gross, Rössler, Merikangas.
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